The Ageing Vascular System

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Aim and layout

Project aim: to analyse and model the effects of age on pulse wave propagation within the cardiovascular system by means of numerical methods.

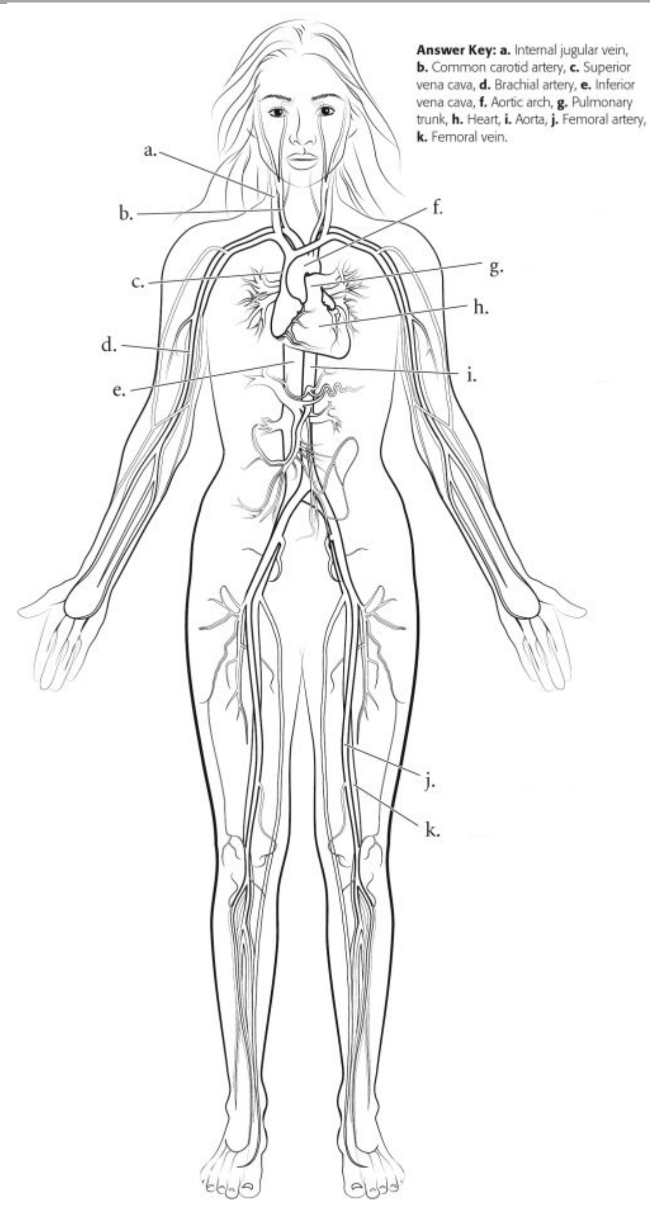
Presentation layout

- Introduction
  - Physiology of the vascular system.
  - Pulse wave propagation and velocity.
  - Clinical relevance.
- Methodology
  - Fluid dynamics fundamental concepts and equations.
  - Dimensionality reduction and trade-offs.
- Future plans

Cardiovascular system

- Heart (4 chambers/4 valves pump).
- Systemic/pulmonary circulation.

1. Aorta, large arteries, small arteries, arterioles, capillaries (*branching*).
2. Aorta $\longrightarrow$ capillaries: $A\downarrow$, *stiffness*$\uparrow$
3. Pulse pressure propagates *as a wave*.



Cardiovascular system [1].

Pulse wave velocity

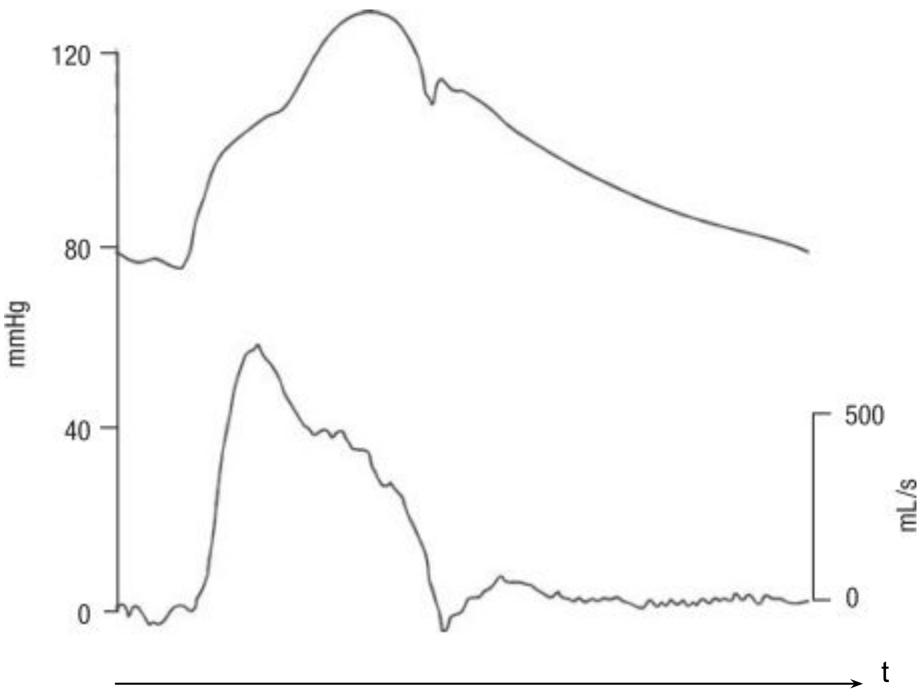
Characterised by the propagation medium (elastic vessel).

- *E* Young's modulus (stiffness).
- *h* wall thickness.
- *r* vessel radius.
- *ρ* blood density.

$$c = \sqrt{\frac{Eh}{2\rho r}}$$

Moens-Kortweg
pulse wave velocity.

Waveforms



Ascending aortic pressure (top) and blood flow velocity (bottom) waves recorded in a human [2].

- Measurement in a point.
- Propagation of pressure through the *entire* system: waves carry information.

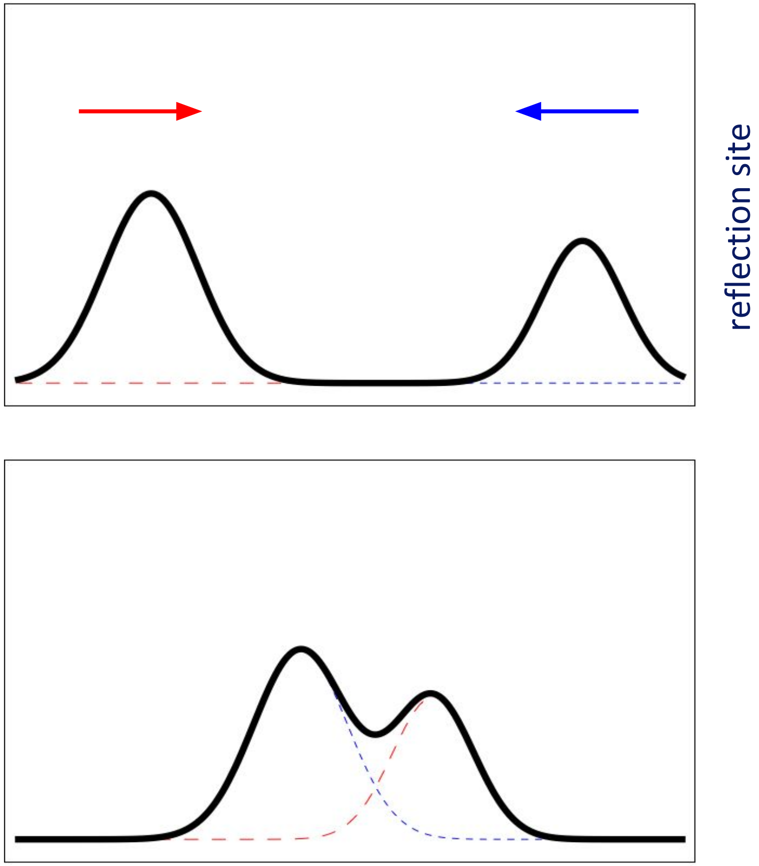
Waves reflection and transmission

Changes in geometry such as:

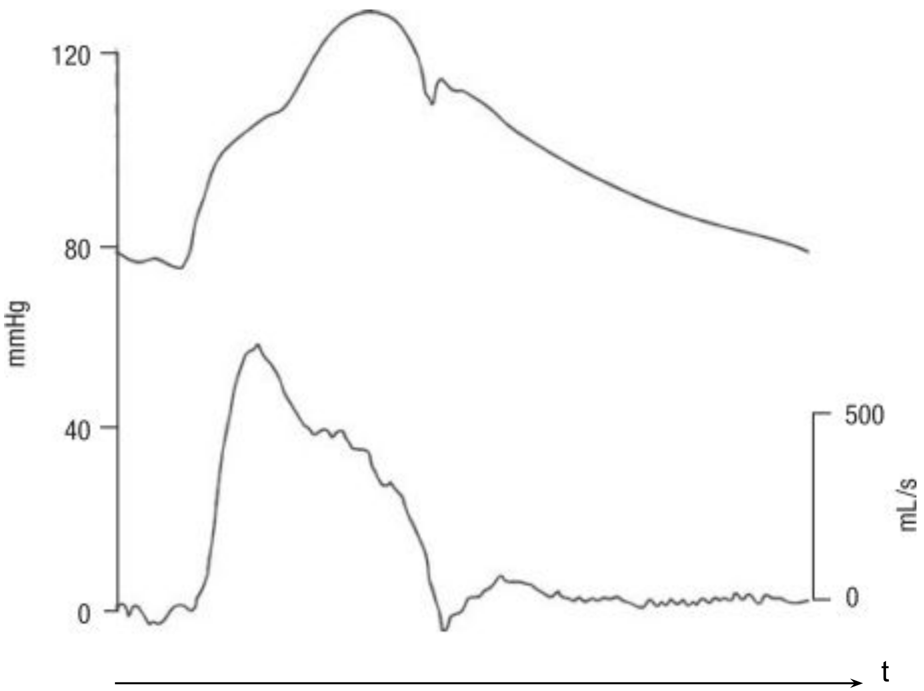
- bifurcations and anastomosis,
- changes in wall thickness,
- tapering,
- changes of stiffness,

constitute *reflection sites*.

The result is the generation of backward travelling waves that interact with forward travelling ones.



Waveforms



Ascending aortic pressure (top) and blood flow velocity (bottom) waves recorded in a human [2].

- Superimposition of forward and backward travelling waves.

Clinical context

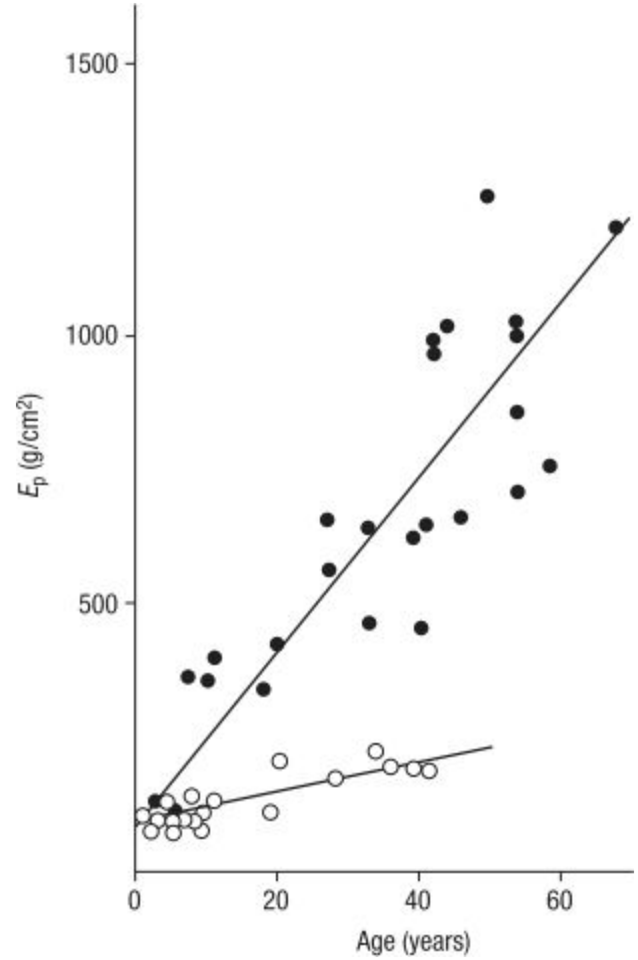
Vascular disorders are primarily related to *arteriosclerosis* (hardening of the arteries) and usually affects all humans as part of the aging process.

Moreover, elastic artery stiffness and wave reflections are increased in patients with:

- *Coronary artery disease* (Gatzka et al., 1998).
- *Myocardial infarction* (Hirai et al., 1989).
- *Hypertension* (Benetos et al., 2002).
- *Stroke* (Lehmann et al., 1995).
- *Diabetes mellitus* (Wilkinson et al., 2000).
- *End-stage renal disease* (Blacher et al., 1999).
- *Hypercholesterolemia* (Wilkinson et al., 2002).

Ageing

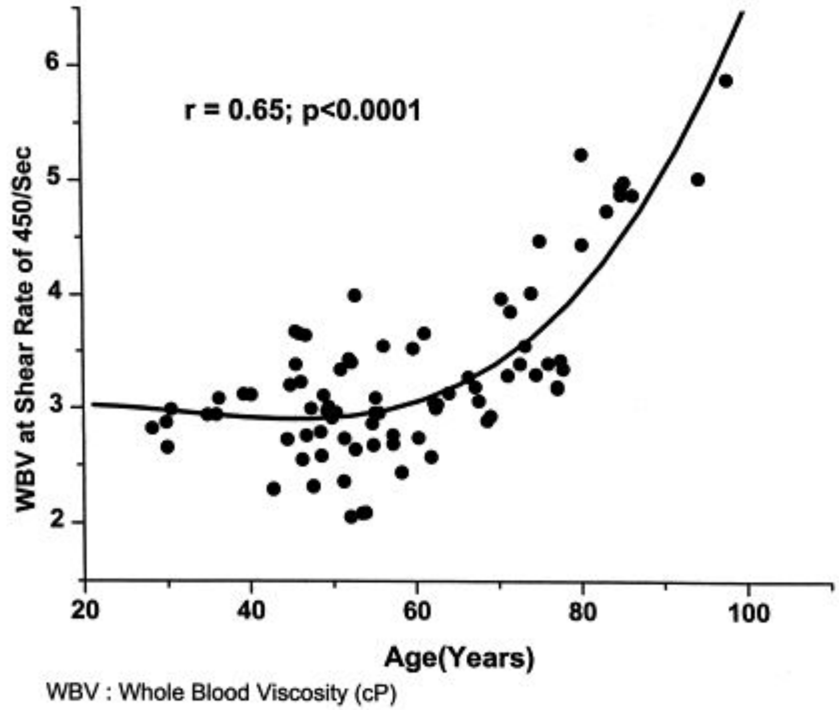
- Wall properties.



Increase in incremental elastic modulus Ep with age in the proximal thoracic aorta (full circle) and proximal pulmonary artery (open circle) of human subjects [2].

Ageing

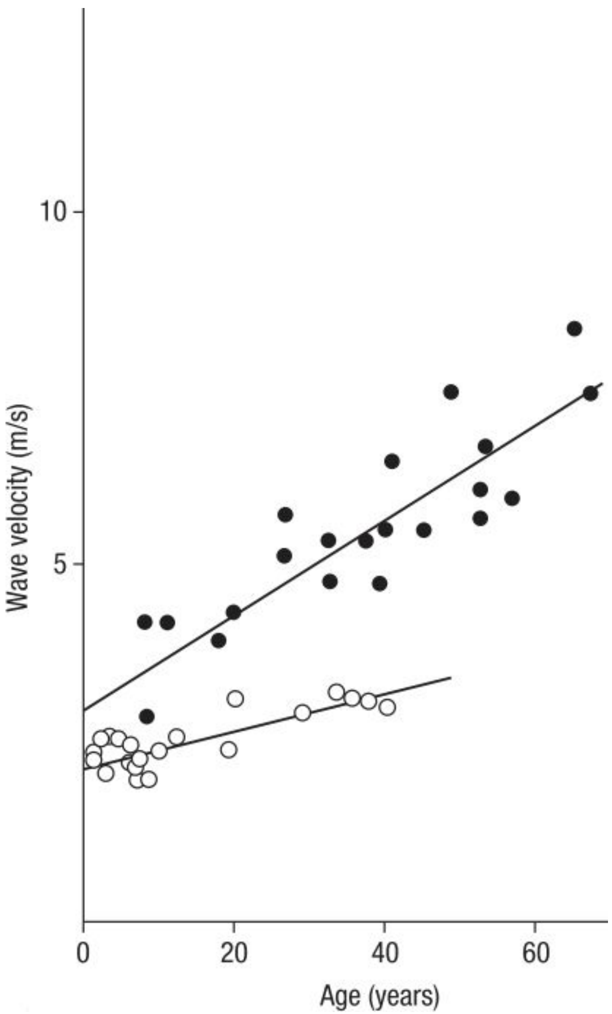
- Wall properties.
- Blood viscosity.



Viscosity measured at a shear rate of 450/sec versus age and the solid line is a fit of the data to a third order polynomial [4].

Ageing

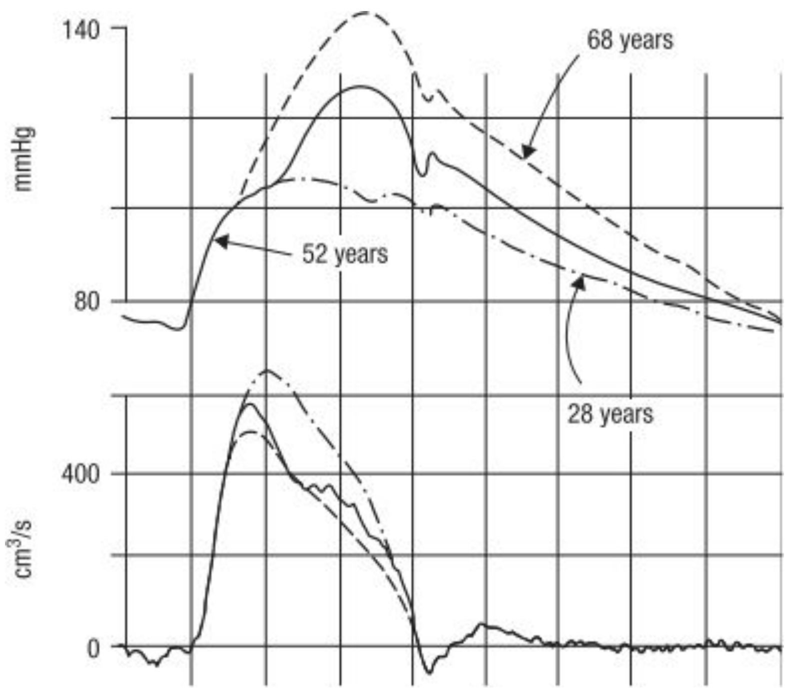
- → Wave velocity.



Increase in pulse wave velocity with age in the proximal thoracic aorta (full circle) and proximal pulmonary artery (open circle) of human subjects [2].

Ageing

- → Waveforms.



Typical pressure and flow waves recorded in three normotensive subjects aged 28, 52, and 68 years [2].

Methodology

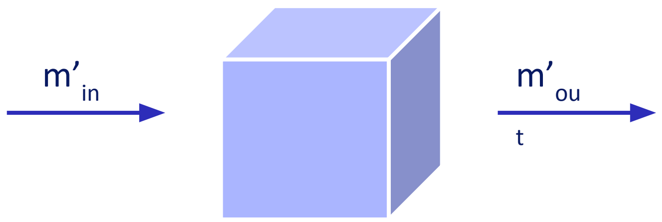
Fundamental principles: conservation laws

- *Mass is conserved* $\longrightarrow$ Continuity equation.
- *Momentum is conserved* $\longrightarrow$ Navier-Stokes equations.
- *Energy is conserved* $\longrightarrow$ Energy equation (rarely used).

Continuity equation

Physical principle: *mass is conserved*.

"...what goes in must come out".

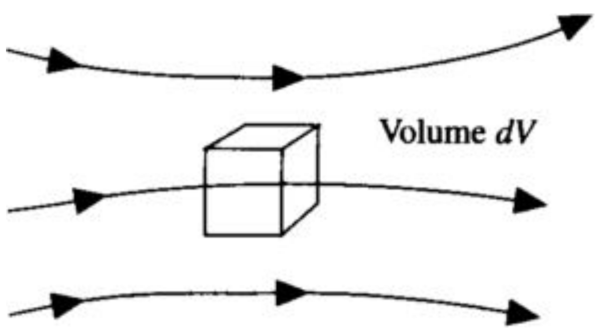


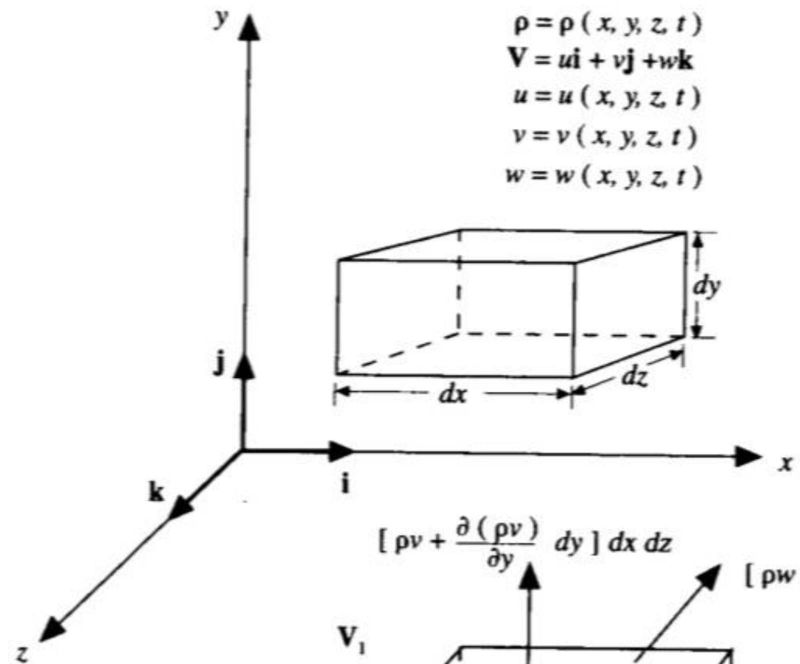
or

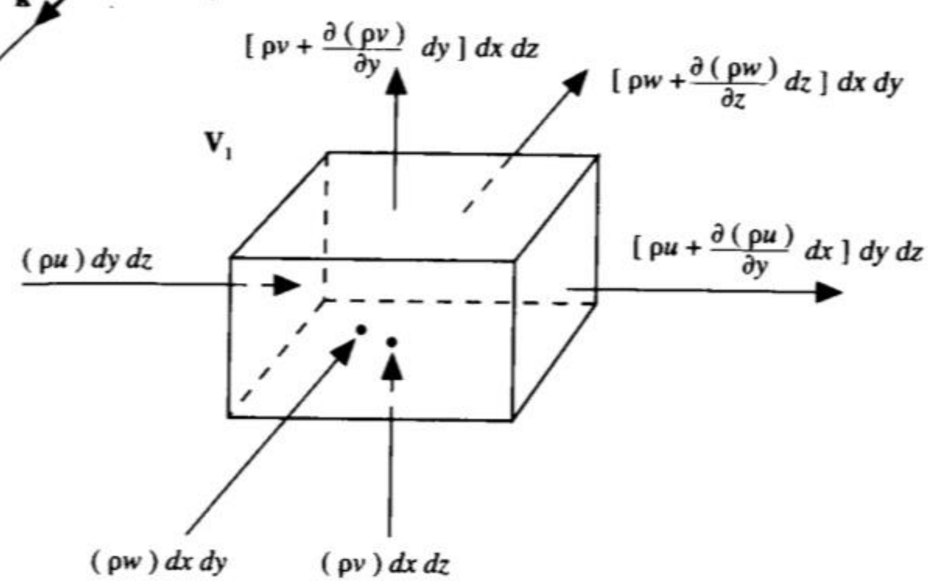
time rate *decrease* of mass inside the element **=** *net* mass flow out the control volume

mass flow: $m' = \rho u A$

net mass flow: $m' = m_{out} - m_{in}$







$$\boxed{\frac{\partial \rho}{\partial t} + \frac{\partial \rho u}{\partial x} + \frac{\partial \rho v}{\partial v} + \frac{\partial \rho w}{\partial z} = 0}$$

Momentum equations

Physical Principle: ***ma*** = ***F***.

mass times the acceleration of the element = *net* force *on* the fluid element

F

Body forces (weight, EM)

Surface forces

Pressure

Viscous

Momentum equations

Physical Principle: ***ma* = *F***.

mass times the acceleration of the element **=** *net* force *on* the fluid element

$$\frac{\partial v_z}{\partial t} + v_z \frac{\partial v_z}{\partial z} + v_r \frac{\partial v_z}{\partial r} + \frac{v_\varphi}{r} \frac{\partial v_z}{\partial \varphi} = -\frac{1}{\rho}\frac{\partial P}{\partial z} + \frac{\mu}{\rho}\left[\frac{\partial^2 v_z}{\partial z^2} + \frac{\partial^2 v_z}{\partial r^2} + \frac{1}{r}\frac{\partial v_z}{\partial r} + \frac{1}{r^2}\frac{\partial^2 v_z}{\partial \varphi^2}\right]$$

$$\frac{\partial v_r}{\partial t} + v_z \frac{\partial v_r}{\partial z} + v_r \frac{\partial v_r}{\partial r} + \frac{v_\varphi}{r} \frac{\partial v_r}{\partial \varphi} - \frac{v_\varphi^2}{r} = -\frac{1}{\rho}\frac{\partial P}{\partial r} + \frac{\mu}{\rho}\left[\frac{\partial^2 v_r}{\partial z^2} + \frac{\partial^2 v_r}{\partial r^2} + \frac{1}{r}\frac{\partial v_r}{\partial r} + \frac{1}{r^2}\frac{\partial^2 v_r}{\partial \varphi^2} - \frac{2}{r^2}\frac{\partial v_\varphi}{\partial \varphi} - \frac{v_r}{r^2}\right]$$

$$\frac{\partial v_\varphi}{\partial t} + v_z \frac{\partial v_\varphi}{\partial z} + v_r \frac{\partial v_\varphi}{\partial r} + \frac{v_\varphi}{r} \frac{\partial v_\varphi}{\partial \varphi} - \frac{v_r v_\varphi}{r} = -\frac{1}{\rho}\frac{\partial P}{\partial \varphi} + \frac{\mu}{\rho}\left[\frac{\partial^2 v_\varphi}{\partial z^2} + \frac{\partial^2 v_\varphi}{\partial r^2} + \frac{1}{r}\frac{\partial v_\varphi}{\partial r} + \frac{1}{r^2}\frac{\partial^2 v_\varphi}{\partial \varphi^2} - \frac{2}{r^2}\frac{\partial v_r}{\partial \varphi} - \frac{v_\varphi}{r^2}\right]$$

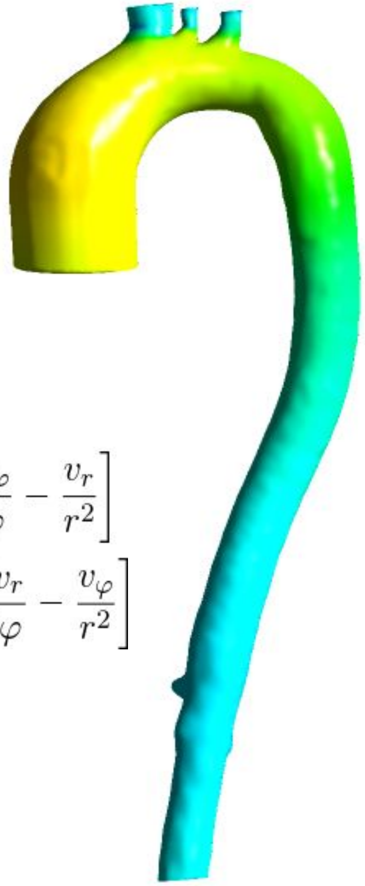
Dimensionality reduction

$$\frac{\partial v_z}{\partial z} + \frac{\partial r v_r}{\partial r} + \frac{1}{r}\frac{\partial v_\varphi}{\partial \varphi} = 0$$

$$\frac{\partial v_z}{\partial t} + v_z\frac{\partial v_z}{\partial z} + v_r\frac{\partial v_z}{\partial r} + \frac{v_\varphi}{r}\frac{\partial v_z}{\partial \varphi} = -\frac{1}{\rho}\frac{\partial P}{\partial z} + \frac{\mu}{\rho}\left[\frac{\partial^2 v_z}{\partial z^2} + \frac{\partial^2 v_z}{\partial r^2} + \frac{1}{r}\frac{\partial v_z}{\partial r} + \frac{1}{r^2}\frac{\partial^2 v_z}{\partial \varphi^2}\right]$$

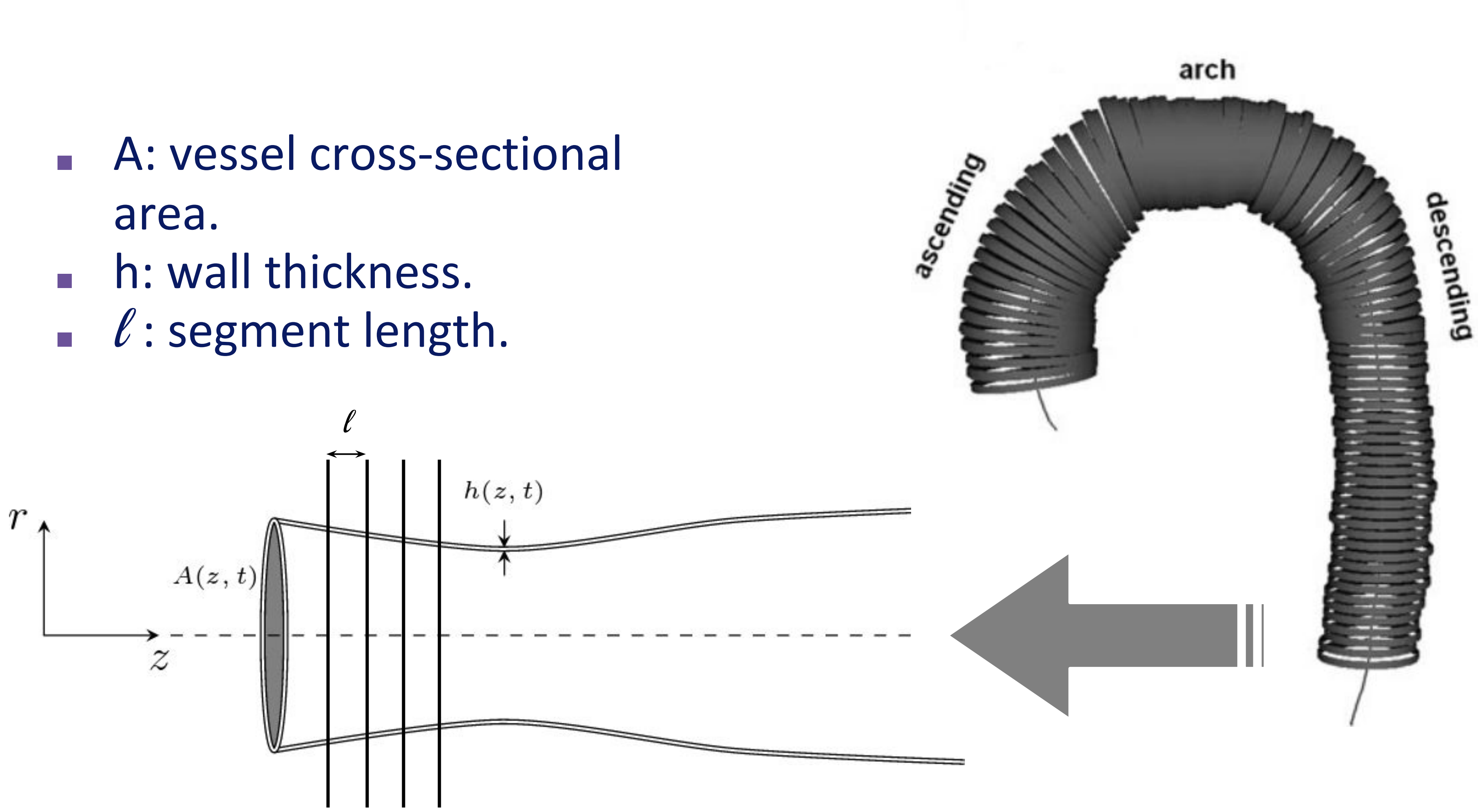
$$\frac{\partial v_r}{\partial t} + v_z\frac{\partial v_r}{\partial z} + v_r\frac{\partial v_r}{\partial r} + \frac{v_\varphi}{r}\frac{\partial v_r}{\partial \varphi} - \frac{v_\varphi^2}{r} = -\frac{1}{\rho}\frac{\partial P}{\partial r} + \frac{\mu}{\rho}\left[\frac{\partial^2 v_r}{\partial z^2} + \frac{\partial^2 v_r}{\partial r^2} + \frac{1}{r}\frac{\partial v_r}{\partial r} + \frac{1}{r^2}\frac{\partial^2 v_r}{\partial \varphi^2} - \frac{2}{r^2}\frac{\partial v_\varphi}{\partial \varphi} - \frac{v_r}{r^2}\right]$$

$$\frac{\partial v_\varphi}{\partial t} + v_z\frac{\partial v_\varphi}{\partial z} + v_r\frac{\partial v_\varphi}{\partial r} + \frac{v_\varphi}{r}\frac{\partial v_\varphi}{\partial \varphi} - \frac{v_r v_\varphi}{r} = -\frac{1}{\rho}\frac{\partial P}{\partial \varphi} + \frac{\mu}{\rho}\left[\frac{\partial^2 v_\varphi}{\partial z^2} + \frac{\partial^2 v_\varphi}{\partial r^2} + \frac{1}{r}\frac{\partial v_\varphi}{\partial r} + \frac{1}{r^2}\frac{\partial^2 v_\varphi}{\partial \varphi^2} - \frac{2}{r^2}\frac{\partial v_r}{\partial \varphi} - \frac{v_\varphi}{r^2}\right]$$



Dimensionality reduction

- A: vessel cross-sectional area.
- h: wall thickness.
- ℓ : segment length.



By expressing the equations in terms of the cross sectional area A, and the flow Q = uA, we obtain

$$\frac{\partial A}{\partial t} + \frac{\partial Q}{\partial z} = 0$$

$$\frac{\partial Q}{\partial t} + \frac{\partial}{\partial z}\left(\alpha \frac{Q^2}{A}\right) + \frac{A}{\rho}\frac{\partial P}{\partial z} = -2\frac{\mu}{\rho}(\gamma + 2)\frac{Q}{A}$$

$$P(A) = \frac{E\sqrt{\pi}h}{A_0(1-\nu^2)}\left(\sqrt{A} - \sqrt{A_0}\right)$$

with α, γ, ν, E, h, A_0 constants.

- 2 equations + 1 constitutive relation.
- 3 unknowns.
- 3 variables to be known for each segment.

By integration between the inlet and outlet we obtain

$$C\frac{\mathrm{d}P_1}{\mathrm{d}t} + Q_2 - Q_1 = 0, \qquad L\frac{\mathrm{d}Q_2}{\mathrm{d}t} + P_2 - P_1 = -RQ_2$$

1 inlet, 2 outlet.

Eventually, for a generic vessel segment (compartment)

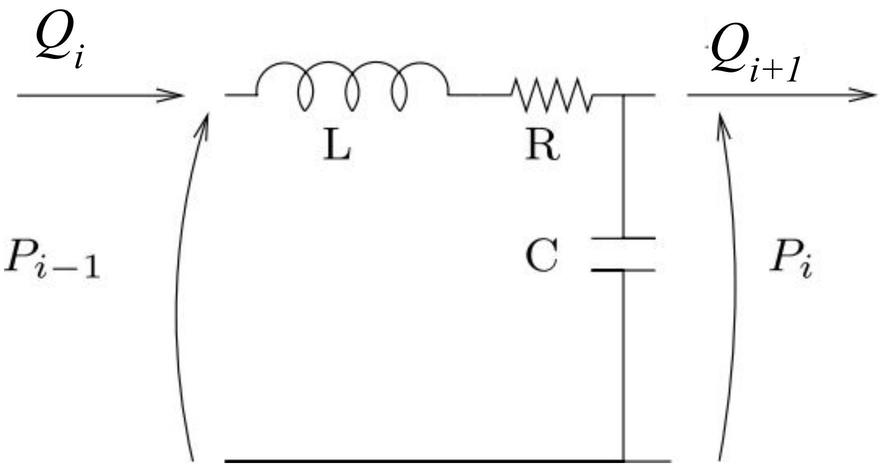
P_{i-1} $\qquad$ P_i

Q_{i-1} $\qquad$ Q_i

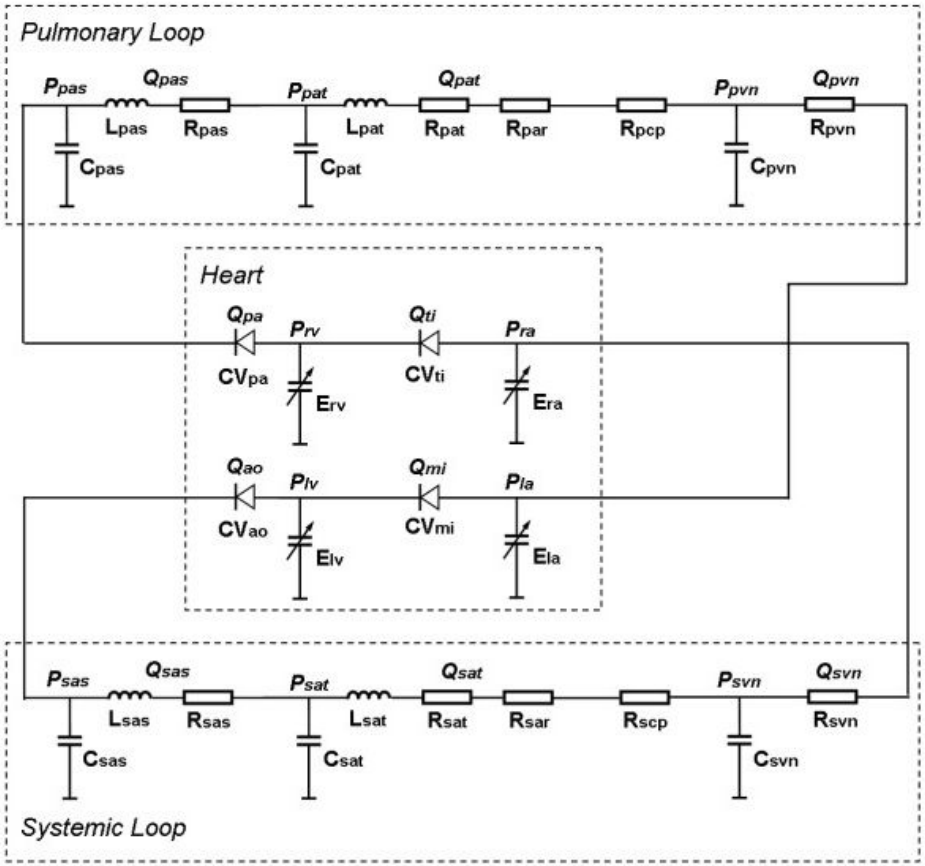
$$\boxed{\begin{aligned} C\frac{dP_{i-1}}{dt} &= Q_{i-i} - Q_i \\ L\frac{dQ_{i-1}}{dt} &= P_{i-1} - P_i - RQ_i \end{aligned}}$$

Lumped parameter (0D) description

- Flow *Q.*
- Pressure *P.*
- Inertance $L = L(\rho,A)$.
- Resistance $R = R(\rho,A,\mu)$.
- Compliance $C = C(A,E,h)$.



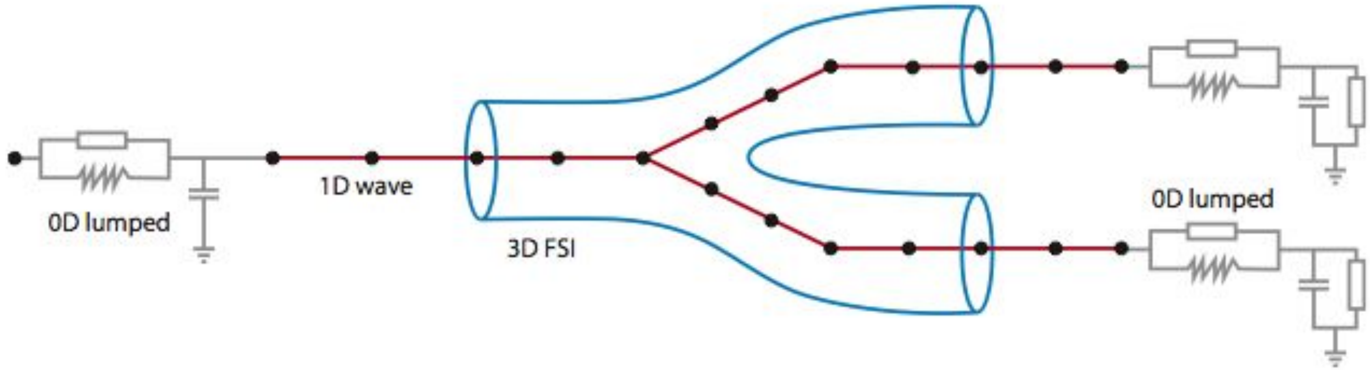
Multi compartment 0D model



A sample complete circulatory system model [9].

	Pros	Cons
3D	★ *Physically accurate* i.e., waves transmission and reflection are modelled directly. ★ Flow solution in every point of the system.	❖ Computationally *expensive*. ❖ Boundary conditions may be difficult to find (needs extremely accurate geometry). ❖ Numerical solution.
1D	★ Simulate pulse wave transmission and *reflection*. ★ Computationally faster than 3D implementation. ★ Provide boundary conditions to 3D models.	❖ *PDE*: numerical solution. ❖ Solution obtained for the vessel mean line under physiological assumptions.
0D (multi-compartment)	★ ODE: *analytical solution*. ★ Computationally efficient. ★ May provide boundary conditions to 1D/3D models. ★ The existing code (state space method) is a novelty.	❖ Parameterization and *calibration* issues. ❖ Loss of physical meaning. ❖ Complex implementation.

Multi scale modelling



Future work

- Parameterisation of existing models.
- Validation with data from literature.
- Comparison 0D vs. 1D.
- Extend to include branching and anastomosis.
- Parameterisation to include age effects on blood and tissues.
- Multi scale model (?).

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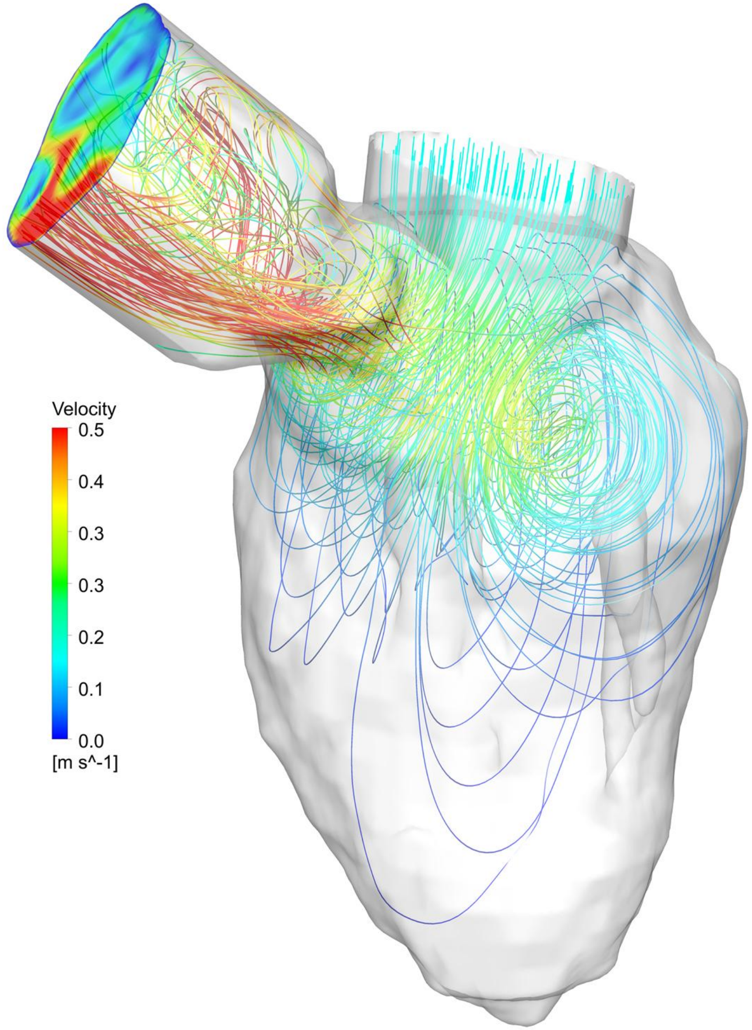
THANK YOU!

Questions?

Arterial flow modelling

Model dimensionality

- 3D
  - Numerical solution.
  - The solution (velocity, pressure, etc..) can be obtained for all the points in the domain.
  - Need to specify accurate boundary conditions and geometry.
  - Aside from numerical errors, it provides a physically correct solution of the problem (transmission and reflection of pressure waves).

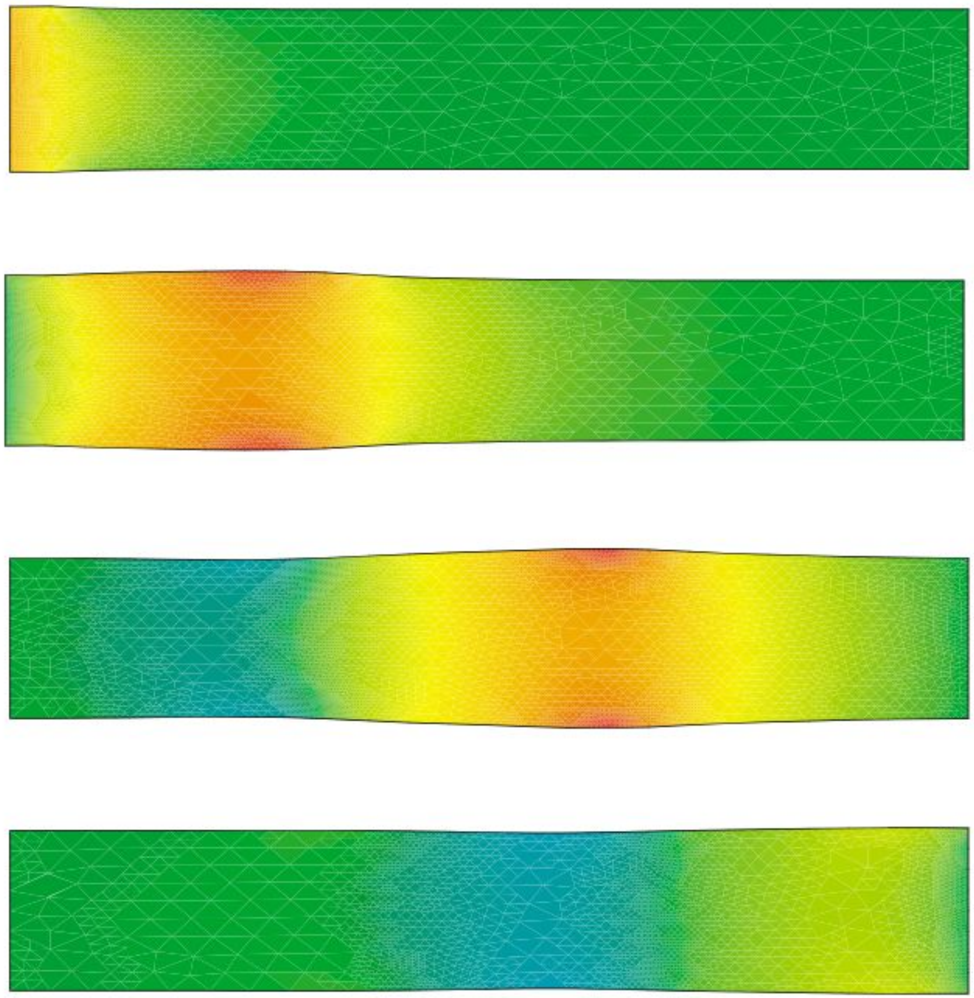


Left ventricle 3D CFD simulation.

Arterial flow modelling

Model dimensionality

- 3D
- 2D
  - Rarely used.
  - Study of the flow along the longitudinal section of the vessel.

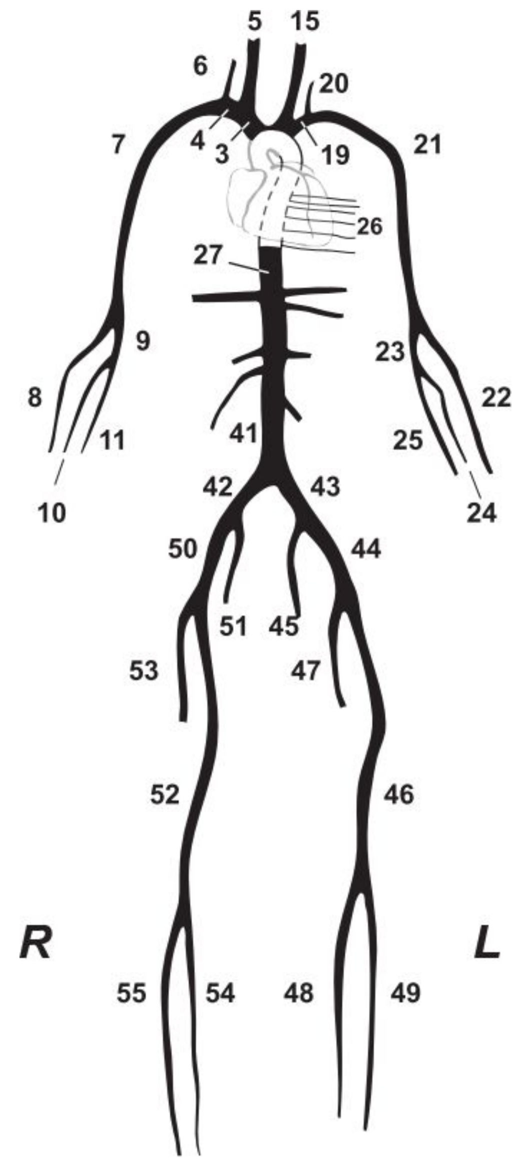


2D simulation of a pressure pulse entering in a generic elastic vessel [13].

Arterial flow modelling

Model dimensionality

- 3D
- 2D
- 1D
  - Simplified equations (assumptions physiologically valid).
  - PDE system which requires numerical solution.
  - Waves transmission and reflection are preserved.
  - Simplified geometry and boundary conditions.

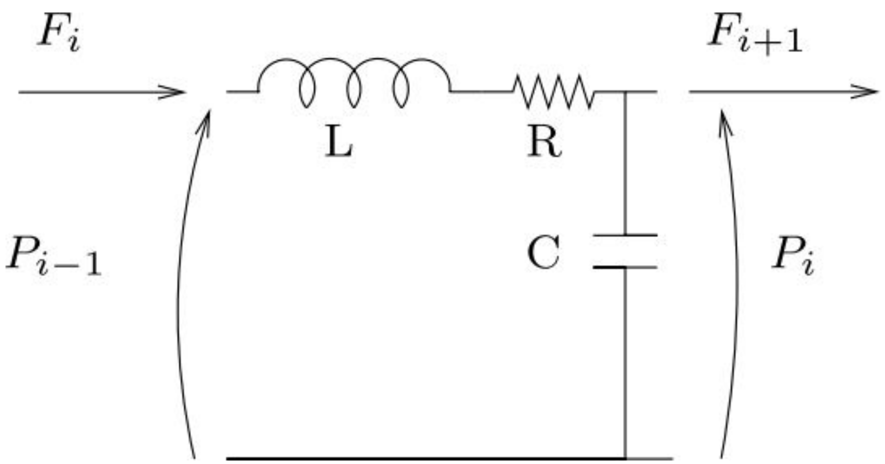


Schematic representation of the arterial tree for 1D blood flow modelling [12].

Arterial flow modelling

Model dimensionality

- 3D
- 2D
- 1D
- 0D
  - ODE system: analytical solution.
  - *May* capture pulse wave transmission *effects*.
  - Loss of physical meaning of the solution.



ℓ circuit [7].